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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,991	01/09/2002	Ian Michael Whitehead	06027.0001U3	7697

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/042,991	WHITEHEAD ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants amendment of claims 1-3, and the addition of claims 16-21, Paper of 9/11/2003, is acknowledged.

Applicants' arguments filed on 9/11/20039, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 1-21 are at issue and are present for examination.

Claim Objections

Claims 1-3 are objected to because of the following informalities:

Newly amended claims 1-3 (4-15 dependent on) are objected to for the recitation of "wherein the amino acid sequence of the recombinant protein is present in a fatty acid 13-hydroperoxide lyase isolated from *Psidium guajava*" because it is confusing if in applicants recitation applicants intend the "amino acid sequence of the recombinant protein" to refer to the full length amino acid sequence of the fatty acid 13-hydroperoxide lyase isolated from *Psidium guajava* or if it is applicants intent that the "amino acid sequence of the recombinant protein" refers to the amino acid sequence set forth in SEQ ID NO: 1, which directly precedes this recitation. For the purpose of advancing prosecution this recitation is interpreted as it intends to refer to the full-length amino acid sequence of the referred to recombinant protein. An amendment such as "**and** wherein the amino acid sequence of the recombinant protein is present in a fatty

acid 13-hydroperoxide lyase isolated from *Psidium guajava*" would overcome this objection.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 and 16-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection was stated in the previous office action and repeated below for applicants convenience.

Claims 1-15 are indefinite in the recitation of "fatty acid 13-hydroperoxide lyase" as the specification defines a "fatty acid 13-hydroperoxide lyase" as a lyase protein having at least one function exhibited by native 13-hydroperoxide lyase, including catalytic activity as well as antigenic activity (see specification, page 5, lines 21-30). This definition of what applicants consider to be encompassed by the term "fatty acid 13-hydroperoxide lyase" is contrary to that which one of skill in the art would consider to be encompassed by the term. The ordinary artisan would consider a "fatty acid 13-hydroperoxide lyase" to have at the minimum enzymatic or catalytic activity, which as defined by the specification is not essential for the described protein, only an option.

Claims 16-21 are included in this rejection for the same reasons as previously discussed for clams 1-15.

In response to this rejection applicants have stated that they agree that one of skill in the art would understand the term "fatty acid 13-hydroperoxide lyase" to encompass enzymatic activity as intended by applicants, however in spite of applicants stated intentions, the claim remains indefinite given applicants specification as recited above. Thus the rejection is maintained. It is suggested that an amendment such as "said recombinant protein has fatty acid 13-hydroperoxide lyase activity" would overcome this rejection and for the sake of advancing prosecution, this is how the rejected claims are interpreted.

Claims 16-18 (19-21 dependent on) are indefinite in the recitation of "stringent hybridization conditions" as the specification does not define what conditions constitute "stringent". While pages 9-10 of the specification describes some conditions which are intended to be stringent, there is nothing to suggest that other conditions would not also be included within the scope of this term and in the art what is considered stringent varies widely depending on the individual situation as well as the person making the determination and thus those molecules encompassed by the set of molecules which will specifically hybridize to SEQ ID NO: 7 and do not hybridize to SEQ ID NOs: 11 or 12 changes dependent on the "stringent conditions" used. As such it is unclear how homologous to the sequence of a gene encoding SEQ ID NO:7, a sequence must be to be included within the scope of these claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-3 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is hereby withdrawn, given applicants argument and the above (See 112 second paragraph rejection) discussed interpretation that the claimed recombinant proteins must have fatty acid 13-hydroperoxide lyase activity. This includes those recombinant proteins of claims 16-21 also.

Claims16-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those claimed methods of use of a 13-hydroperoxide lyase enzyme wherein said polypeptide comprises the amino acid sequence of SEQ ID NOs: 2, 3, 4, or 6, does not reasonably provide enablement for those claimed methods of use of a 13-hydroperoxide lyase enzyme encoded by a nucleic acid, wherein said nucleic acid specifically hybridizes with the nucleic acid of SEQ ID NO: 7 under stringent conditions (See also above 112 2nd paragraph rejection) and does not hybridize under stringent conditions to the nucleic acid set forth in SEQ ID NO: 11 or SEQ ID NO: 12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-3 which were previously included in this rejection have been withdrawn from the rejection based on applicants argument and the interpretation of the claims as discussed above under 112 second paragraph rejection. Applicants argument as presented with respect to claims 1-3 does not apply to newly added claims 16-21 which remain rejected.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 16-21 are so broad as to encompass the any method of use of a 13-hydroperoxide lyase enzyme encoded by a nucleic acid, wherein said nucleic acid specifically hybridizes with the nucleic acid of SEQ ID NO: 7 under stringent conditions (See also above 112 2nd paragraph rejection) and does not hybridize under stringent conditions to the nucleic acid set forth in SEQ ID NO: 11 or SEQ ID NO: 12. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the methods of use of the extremely large number of enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of

and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to those methods of use of those polypeptides having 13-hydroperoxide lyase enzymatic activity wherein said polypeptide comprises the amino acid sequence of SEQ ID NOs: 2, 3, 4, or 6.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass those methods of use of any polypeptide mutant or fragment of any 13-hydroperoxide lyase encoded by a nucleic acid, wherein said nucleic acid specifically hybridizes with the nucleic acid of SEQ ID NO: 7 and does not hybridize to the nucleic acid set forth in SEQ ID NO: 11 or SEQ ID NO: 12, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting 13-hydroperoxide lyase enzymatic activity; (B) the general tolerance of 13-hydroperoxide lyases to modification and extent of such tolerance; (C) a rational and

predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the 13-hydroperoxide lyase activity necessary to practice the claimed methods and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides having the necessary 13-hydroperoxide lyase activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any 13-hydroperoxide lyase, so long as the polypeptide is encoded by a nucleic acid, wherein said nucleic acid specifically hybridizes with the nucleic acid of SEQ ID NO: 7 and does not hybridize to the nucleic acid set forth in SEQ ID NO: 11 or SEQ ID NO: 12. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily,

and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Remarks

No claim is allowed.

Conclusion

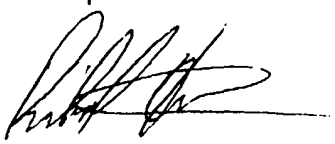
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
November 25, 2003